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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/662,441      | 09/16/2003  | Finn Myhren          | 063779-5001         | 9826             |

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WASHINGTON, DC 20004

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| EXAMINER |
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BADIO, BARBARA P

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| ART UNIT | PAPER NUMBER |
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1617

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| MAIL DATE | DELIVERY MODE |
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07/26/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

Application No.

10/662,441

Applicant(s)

MYHREN ET AL.

Examiner

Barbara P. Badio, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213..

## Disposition of Claims

- 4) ☒ Claim(s) 56-119 is/are pending in the application.
- 4a) Of the above claim(s) 62,63,66,68,74,75,77,79,84,86 and 90-119 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 56-61,64,65,67,69-73,76,78,80-83,85 and 87-89 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 September 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☒ Certified copies of the priority documents have been received in Application No. 10/116,358.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 12/18/2003.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_.

**First Office Action on the Merits**

***Election/Restrictions***

1. Applicant's election of Group I in the reply filed on June 22, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
2. Based on applicant's election of Group I and the compounds as defined in the reply filed June 22, 2007, claims 62, 63, 66, 68, 74, 75, 77, 79, 84, 86 and 90-119 have been withdrawn from further consideration as being drawn to a nonelected invention/species. Claims 56-61, 64, 65, 67, 69-73, 76, 78, 80-83, 85 and 87-89 will be examined according to MPEP § 803.02.

***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:  

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
4. Claims 56-61, 64, 65, 67, 69-73, 76, 78, 80-83, 85 and 87-89 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that

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the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to the treatment of cancer utilizing a cytotoxic agent linked to a lipophilic moiety. The present specification describes derivatisation of biologically active compounds with  $\omega$ -9 C18 or C20 monounsaturated fatty acid and set forth specific lipophilic moieties (see page 4, lines 11-20). The present specification does not reasonably convey to the skilled artisan in the art that applicant, at the time the present application was filed, had possession of compounds linked to other lipophilic moieties as encompassed by the instant claims.

5. Claims 56-61, 64, 65, 67, 69-73, 76, 78, 80-83, 85 and 87-89 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific lipophilic groups found on page 4, lines 11-20, does not reasonably provide enablement for all lipophilic groups. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are (1) the nature of the invention, (2) the breadth of the claims, (3) the state of the prior art, (4) the predictability or unpredictability of the art, (5) the amount of guidance or direction presented, (6) the presence or absence of working examples, (7) the relative skill in the

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art and (8) the quantity of experimentation necessary. When the above factors are taken into consideration, the examiner's position is that one skilled in the art could not perform the invention commensurate in scope with the instant claim without undue experimentation.

Briefly, the instant claims are drawn to a method of treating cancer utilizing a cytotoxic agent covalently bonded to a lipophilic moiety. Thus, the instant claims are drawn to the utilization of any cytotoxic agent linked to any lipophilic moiety. However, the present specification discloses the derivatisation utilizing  $\omega$ -9 C18 or C20 monounsaturated fatty acids and set forth specific lipophilic moieties for production of the compounds useful in the claimed invention (see for example page 4, lines 11-20). The present specification lacks description/definition of other lipophilic moieties that would be useful in the claimed invention and, thus, does not enable the skilled artisan in the art to make and/or use the invention commensurate in scope with the instant claims.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 67, 78 and 85 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims recite, "the covalent bond is in a position to improve activity and transport of the drug into a cell". It is unclear what is intended by the phrase because the present specification lacks definition/identification of said position(s).

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***Claim Rejections - 35 USC § 102***

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 57-61, 64, 65, 67, 72, 73 and 76 are rejected under 35 U.S.C. 102(b) as being anticipated by Aszalos et al. (Biochemical Pharmacology, 1995).

Aszalos et al. teaches the antitumor activity of N-acylated daunorubicins (see the entire article, especially Abstract and page 889, Results and Discussion). The reference teaches that longer fatty acid derivatives, such as N-octanoyl and N-dodecanoyl daunorubicins, were not substrates for P-glycoprotein, a cause of resistance to chemotherapeutic agents (see page 889, col. 1, 1<sup>st</sup> paragraph). The method of use taught by the reference is encompassed by the instant claims.

***Claim Rejections - 35 USC § 103***

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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11. Claims 56-61, 64, 65, 67, 69-73, 76, 78, 80-83, 85 and 87-89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aszalos et al. (Biochemical Pharmacology, 1995).

Aszalos et al. teaches the antitumor activity of N-acylated daunorubicins (see the entire article, especially Abstract and page 889, Results and Discussion). The reference teaches that longer fatty acid derivatives, such as N-octanoyl and N-dodecanoyl daunorubicins, were not substrates for P-glycoprotein, a cause of resistance to chemotherapeutic agents (see page 889, col. 1, 1<sup>st</sup> paragraph).

The instant claims differ from the reference by reciting additional lipophilic derivatives of daunorubicin, for example, the C-18 unsaturated fatty acid derivatives. However, Aszalos teaches longer fatty acid overcome the resistance caused by over expression of P-glycoprotein in cancer cells. Therefore, the skilled artisan in the art would have been motivated to produce other N-acylated derivatives of daunorubicins utilizing other longer fatty acids with the reasonable expectation that the compounds produced would not be substrates for P-glycoprotein and, thus, be useful in treating patients with resistance to daunorubicin.

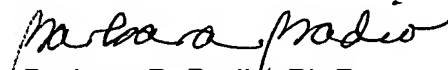
### ***Telephone Inquiry***

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Barbara P. Badio, Ph.D. whose telephone number is 571-272-0609. The examiner can normally be reached on M-F from 6:30am-4:00pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan-Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

  
(Barbara P. Badio, Ph.D.)  
Primary Examiner  
Art Unit 1617

BB  
July 23, 2007